

### **REMARKS**

The Office Action mailed July 28, 2003, has been received and reviewed. Claims 1 through 12, 14, 15, and 17 through 26 are currently pending. Claims 1 through 12, 14, 15, and 17 through 26 were rejected. Claims 1 and 17-26 are currently amended. All claim amendments and cancellations are made without prejudice or disclaimer. Reconsideration is respectfully solicited.

#### **Telephonic Interview**

Applicant would like to thank Examiner Strzelecka for the courtesy extended to applicant's representative Roula Thomas during the telephonic interview held on October 22, 2003. The telephonic interview was found to be helpful in understanding the Office's positions relative to patentability of the present application, as reflected in the foregoing amendments and the discussion that follows.

#### **Claim objections**

The Office objected to the claim language "primer-specific" in claims 1 and 20. The Office also objected to claim 20 because it contained a repeat of the claim language "ddNPTs".

Claims 1 and 20, as well as claims 17-19 and 21-26, have been amended to change "primer-specific" to "primer specific". In addition, claim 20 has been amended to delete the repeated claim language "ddNPTs". It is respectfully submitted that these amendments overcome all claim objections of record.

#### **Matters relating to 35 U.S.C. § 112**

In the telephonic interview of October, 22, 2003, the Examiner asserted that the present application fails to provide sufficient support for the subject matter of independent claims 1, 20, 23 and 24. The Examiner asserted that, although the specification does provide enabling support for the termination of primer extension with one or two mispairs, the present application does not

provide enabling results data to support *mispaired primer extension*. Applicant respectfully disagrees and submits that the specification does, in fact, provide enabling support for the subject matter of the presently pending claims.

For instance, paragraph [0061] of the specification teaches that extension beyond mispairs allows for the identification of a single point mutation or variation with the assay of the present invention. FIG. 1 provides supporting results data for the termination of primer extension with one or two mispairs and further provides results data for *mispaired extension*.

More specifically, referring to the gels shown in FIG. 1 section II and the sequences of sections I', II' and III', it is noted that mispaired extension occurred in lane II-3, where the band shown at 98 (C), lane II-3, is for the extension product comprising a mispaired extension past mispair (A)-(C), (genotype 1a, primer 1AB); mispaired extension also occurred past an (A)-(C) mispair (genotype 1b, primer 1AB) as shown by the band at 99 (G) in lane II-1; and mispaired extension past a (T)-(G) mispair (genotype 1b, primer 1BR) as supported by the band at 113 (C) in lane II-2. Accordingly, as can be clearly seen in FIG. 1, instead of the termination of primer extension at 108 (G), lane II-2, mispaired primer extension occurred beyond the (T)-(G) mispairing, and primer extension continued until at least two mispairs terminated primer extension at 113 (C).

Based on the teachings of the present application, an ordinarily skilled artisan would know that the termination of primer extension may occur with a single mispair or with at least two mispairs, but also that the present application is additionally directed to mispaired extension. Therefore, the present application and the results data provided therein support the claimed assays' ability to examine both primer specific *paired extension* and primer specific *mispaired extension* for the determination of a complete genotypic profile. Accordingly, the primer specific mispair extension assay of the present invention is capable of discriminating between genotypes and is a novel genotyping assay that inventively examines the accuracy and inaccuracy of *Pfu* in primer extension and termination.

In the telephonic interview of October 22, 2003, the Examiner asserted that it may be

difficult for one skilled in the art to easily locate results data relating to mispaired extension. The specification has been amended to more readily guide the reader's attention to the appropriate results data. Specifically, to clarify a reference in the specification to the drawings, paragraph [0060] has been amended to include the language "as shown in FIG.1, columns II-1, II-2 and II-3". To provide further clarification, FIG.1 has been amended to correlate the sequences of sections I', II' and III' to their corresponding lanes in columns I, II, and III. No new subject matter has been added.

It is respectfully submitted that the present application complies with all the requirements of 35 U.S.C. § 112.

### **Rejections under 35 U.S.C. §§ 102/103**

Inherent Anticipation Rejection Based on PCT International Patent Publication WO 96/30545 to Fahy - Alternative Obviousness Rejection Based on Fahy in view of Lundberg KS et al. (1991), "High-fidelity amplification using a thermostable DNA polymerase isolated from *Pyrococcus furiosus*," *Gene* vol. 108, pages 1-6

Claims 1 through 11, 14-15, and 17 through 26 were rejected under 35 U.S.C. § 102(b) as being assertedly inherently anticipated by PCT International Patent Publication WO 96/30545 to Fahy (hereinafter "Fahy") and, in the alternative, under 35 U.S.C. § 103(a) as being assertedly obvious over Fahy in view of Lundberg KS et al. (1991), "High-fidelity amplification using a thermostable DNA polymerase isolated from *Pyrococcus furiosus*," *Gene* vol. 108, pages 1-6 (hereinafter "Lundberg"). The rejection is respectfully traversed, as set forth below.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Brothers v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, the identical invention must be shown in as complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Additionally, the elements must be arranged

as required by the claim. *In re Bond*, 15 USPQ2d 1566 (Fed. Cir. 1990); *see generally* MPEP § 2131.

MPEP §§ 706.02(j) and 2143 set forth the standard for an obviousness rejection:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Although the Office may rely on the inherent teachings of a reference in making a rejection based on anticipation or obviousness, to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is *necessarily* present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient. MPEP § 2112; *In re Robertson*, 169 F.3d 743, 745 (Fed. Cir. 1999) (emphasis added).

The Office correctly noted that "Fahy does not teach termination of extension products in the presence of at least two mispairs within a 2 to 4 base pair range located downstream of the 3' end of the primer or termination of extension products in the presence of a mispair occurring at at least one of a first or second base pair immediately adjacent to the 3' end of the primer." Office Action, page 4. Nevertheless, the Office relied on the teachings of Lundberg in asserting that "the position of a mispair formation with respect to the 3' end of the primer is dependent on the template sequence and type of dNTPs present in the reaction mixture, and is inherently related to the fact that *Pfu* polymerase is a high-fidelity polymerase." Id. The Office then rejected claims 1 through 11, 14, 15, and 17 through 26 as being either inherently anticipated by Fahy or, in the alternative, obvious over Fahy in view of Lundberg.

It is respectfully submitted that neither Fahy nor Lundberg, alone or in combination, teaches an assay using primer specific *paired* extensions and primer specific *mismatched* extensions to determine specific genotype profiles. Moreover, at the time of the present invention, it was not recognized in the art that use of *Pfu* polymerase would *necessarily* result in termination of primer extensions in the presence of at least 2 mismatches within a 2 to 4 base pair range located downstream of the 3' end of the primer or termination of extension products in the presence of a mismatch occurring at at least one of a first or second base pair immediately adjacent the 3' end. Therefore, Fahy neither inherently anticipates the subject claims nor renders the subject claims obvious in view of Lundberg.

In addition, neither Fahy nor Lundberg, alone or in combination, clearly defines *where* extension termination will occur. That is to say, Fahy and Lundberg do not describe termination of extension when mismatching occurs "within a 2 to 4 base pair range located downstream of the 3' end of the primer" or "at at least one of a first or second base pair immediately adjacent to the 3' end of the primer". Fahy and Lundberg therefore do not and cannot lead an ordinarily skilled artisan to ascertain the specific site of termination relative to the 3' end of the primer, as recited in the subject claims.

It is respectfully asserted that neither Fahy nor Lundberg provides any teaching of the use of a high-fidelity DNA polymerase, or *Pfu*, in a primer specific *mismatched* extension assay. Further, Fahy and Lundberg fail to teach the ability of *Pfu* to extend beyond a mismatch.

Accordingly, Fahy does not inherently anticipate claims 1 through 11, 14, 15, and 17 through 26, nor does the asserted combination of Fahy and Lundberg render these claims obvious. Withdrawal of the rejection is therefore respectfully solicited.

### **Rejections under 35 U.S.C. § 103(a)**

#### Obviousness Rejection Based on Fahy in view of Lundberg and U.S. Patent 5,527,669 to Resnick

Claim 12 was rejected under 35 U.S.C. § 103(a) as being assertedly obvious over Fahy in view of Lundberg and U.S. Patent 5,527,669 to Resnick et al. (hereinafter "Resnick"). As

discussed above, claim 1 is neither anticipated nor rendered obvious by Fahy and Lundberg because the cited references fail to describe, expressly or inherently, all the limitations of claim 1. The teachings of Resnick do not provide the subject matter omitted by Fahy and Lundberg. Accordingly, claim 12 is necessarily patentable over the cited references because it depends from claim 1. Withdrawal of the rejection is therefore respectfully requested.

Obviousness Rejection Based on Fahy in view of Lundberg and U.S. Patent 5,550,016 to Okamoto

Claim 12 was also rejected under 35 U.S.C. § 103(a) as being assertedly obvious over Fahy in view of Lundberg and U.S. Patent 5,550,016 to Okamoto (hereinafter "Okamoto"). As discussed above, claim 1 is neither anticipated nor rendered obvious by Fahy and Lundberg because the cited references fail to describe, expressly or inherently, all the limitations of claim 1. The addition of the teachings of Okamoto does not provide the subject matter omitted by Fahy and Lundberg. Accordingly, claim 12 is necessarily patentable over the cited references because it depends from claim 1. Withdrawal of the rejection is therefore respectfully requested.

### CONCLUSION

It is believed that claims 1 through 12, 14, 15, and 17 through 26, as amended, are in condition for allowance, and timely issuance of a Notice of Allowance in this case is therefore respectfully requested. Should the Office determine that additional issues remain which might be resolved by a telephone conference, it is respectfully invited to contact applicants' attorney of record at the address or telephone number given herein.

Respectfully submitted,



Shawn G. Hansen  
Registration No. 42,627  
Attorney for Applicants  
TRASKBRITT, P.C.  
P.O. Box 2550  
Salt Lake City, Utah 84110-2550  
Telephone: 801-532-1922

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Enclosures: **Appendix A** (replacement drawing sheets)

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